De structurele basis van de antilichaamspecifiteit

Seijen, Hendrik Geert

SUMMARY

The work described in this thesis was aimed at establishing the chemical basis of antibody specificity, i.e. to answer the question whether antibodies of different specificities possess the same or different amino acid sequences in their combining sites. As elucidation of the total sequences of a number of antibodies seemed beyond reach, we used specific (papain) fragmentation of the antibodies and peptide mapping of the fragments to analyse their structural features.

Chapter I, an introductory chapter, describes relevant features of the antigen-antibody reaction and the structure of immunoglobulin G. Special consideration is given to the different forms of heterogeneity of immunoglobulin G: heterogeneity in electrophoretic and chromatographic properties, in antigenic determinants, and in antigen-binding capacity. The end of the chapter discusses the structural problems of antibodies.

The papain fragments of immunoglobulin G from non-immunized, immune, and hyperimmune rabbits were subjected to fingerprinting after performic acid oxidation and trypsin splitting. The results (Chapter III) clearly show that all antibodies, notwithstanding differences in specificity, to a large extent possess identical amino acid sequences. The number of strongly staining peptides was in agreement with that expected for the four-chain, symmetrical model of immunoglobulin G. The total number of peptides, however, exceeded the expected number; this shows that at least some heterogeneity in amino acid sequence must be present.

The fingerprints of antibodies against a positively charged hapten (p-azo-phenyltrimethylammonium chloride) and against two negatively charged haptens (p-azobenzoic acid and m-azobenzoic acid) (Chapter IV) were, to our surprise, not different from those of normal immunoglobulin G, which is a mixture of a very large number of antibodies. We have thus to conclude that either all antibodies

possess the same amino acid sequences - which we consider, to say the least, highly impropable - or that we failed to detect peptide differences. This failure cannot be due to technical causes, and our haptens were so chosen as to make detectibility of differences maximal. We have, therefore, to conclude (Chapter V) that antibodies against even a single antigenic determinant are populations of molecules with different amino acid sequences in their combining sites.

In our view the antigen acts selectively by inducing the formation of a population of fitting antibodies.